

The Washington Post

Volunteers at Walter Reed endure mosquito bites to help find a malaria vaccine

By Eric Niiler

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Jesse Bolton is a pretty buff guy. He's in the Navy, and a few mosquitoes don't scare him much. But he has seen what the bite of a malaria-carrying insect can do. One of his squadmates picked it up in Africa a few years ago.

That's why Bolton was sitting in a suite at the Residence Inn in Bethesda in June, getting ready to give a blood sample. As part of a scientific experiment, Bolton had allowed himself to be bitten by a pretty buff mosquito.

"These mosquitoes were huge," said Bolton, 27, a medical technician at the National Naval Medical Center in Bethesda. "Probably with legs that were the size of a quarter."

Now, 10 days after the bite, he was sweaty, tired and registering a 102-degree fever, signs that a malaria parasite was doing a number on his bloodstream.

Bolton was one of a dozen volunteers being monitored by doctors and nurses from the Walter Reed Army Institute of Research. The entire sixth floor of the hotel had been rented and turned into a care unit, laboratory and doctor's office. For two weeks, professionals drew blood and checked on the parasite's progress. Each time blood was drawn, the volunteers got a crisp \$100 bill; once any of

them exhibited symptoms, they were quickly treated with malaria medication. They will be monitored for the next six months to be sure the disease doesn't recur.

For the past 17 years, Walter Reed's "human challenge model," in which volunteers get bitten by malaria-carrying mosquitoes, has been a critical tool in the global war against malaria. Some trials have tested medicines to treat patients; others test vaccines to prevent people from getting the disease. Bolton's was aimed simply at showing that researchers could infect people with *Plasmodium vivax*, one of the five strains of the malaria parasite.

"The goal is to show that we can reliably establish malaria infection in healthy individuals," says Col. Chris Ockenhouse, director of Walter Reed's malaria vaccine program. "By doing this, we have a tool to

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test drugs and vaccines."

Malaria, whose symptoms include a cycle of severe chills and fever, is a stubborn killer responsible for the deaths of nearly 1 million people each year, most of them babies in sub-Saharan Africa. In the United States, federal officials reported 1,300 malaria cases in 2008, with two deaths. But for U.S. travelers to parts of Africa, South America, Asia and the Caribbean -- including members of the military deployed to tropical zones -- malaria remains a persistent threat.

While several medications have been found to treat malaria and prevent its recurrence, there is still no effective vaccine.

16,000 babies

That's why so much is riding on a massive trial underway in Africa. A prospective vaccine called RTS,S was developed in Belgium by GlaxoSmithKline and initially tested on a small number of volunteers in a Walter Reed project in 1997. Today, with the help of \$451 million from the Bill and Melinda Gates Foundation, RTS,S is midway through what researchers describe as the largest and most promising trial in malaria-vaccine history, involving 16,000 babies at 11 sites in seven African countries.

The participants are between 5 and 17 months old; some of them get the vaccine, which is aimed at the *Plasmodium falciparum* strain of the parasite, and others get placebos. Researchers plan to follow the

babies through 2012. Walter Reed is running two of the test sites, both in Kenya.

The Gates foundation has put \$1.4 billion into anti-malaria projects in the past decade, paying for everything from drug development to such low-tech measures as mosquito netting for rural villages. As a result, some African nations have seen malaria rates drop by half. But at the same time, the parasite's resistance to some drugs is growing, while new outbreaks are underway in Venezuela and parts of Southeast Asia.

"We're hoping [the RTS,S vaccine] will be the catalyst for other foundations and governments to start pouring resources into the fight," said Ashley Birkett, pre-clinical research and development director at the Path Malaria Vaccine Initiative, a venture established by Gates that has helped shepherd RTS,S through its development. "We need to show that we can be successful and really give credibility to developing a malaria

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In earlier trials, RTS,S has been shown to protect just more than half the people who receive it. Birkett said the eventual goal is 85 percent protection.

A taste of blood

The long road to this point began more than a decade ago at the Walter Reed insectary, a sort of mosquito hothouse where millions of mosquitoes are bred deep inside a building at the institute's Silver Spring campus. Once through a security checkpoint, visitors and workers pass through seven pressure-sealed doors before reaching a sealed chamber. There, technician Mike Porter was checking racks of mosquito larvae on a recent afternoon, making sure they had enough sugar water for nourishment.

"I do get bit," said Porter, a recent college graduate who hopes to make malaria his career. "But not by the infected ones."

One of Porter's jobs is to separate the adult males from the females -- because it's the females that bite humans and transmit the malaria parasite.

"After a while, you can tell the difference," Porter said. "Females have larger abdomens, males have fluffier antennae."

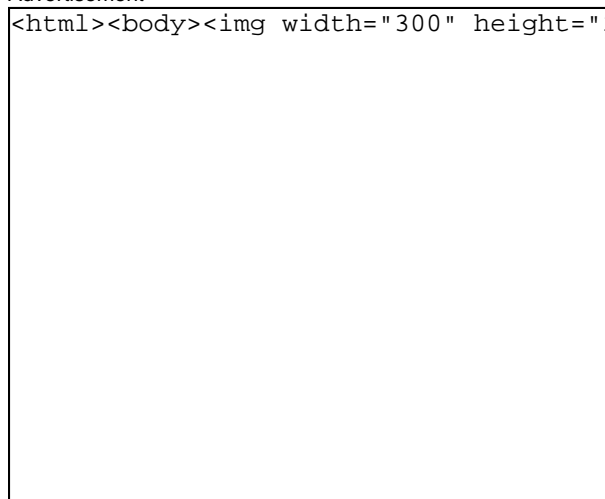
Once separated, the females get a taste of blood containing the malaria parasite. After they bite the human volunteers, the insects

are dissected to make sure they were carrying the parasite. Then the volunteers are off to the Residence Inn for two weeks, spending nights and weekends in their hotel rooms with medical staff just down the hall and heading to work as usual until they get sick and need to be treated.

More than 950 volunteers, mostly civilians, have taken part in the human challenge model over the past 17 years, Ockenhouse said. He said other aspects of Walter Reed's malaria program include a team of Army researchers brewing batches of high-tech bug repellent and a study of molecular structures on *Plasmodium* that might help scientists knock out this stubborn parasite.

"It's an amazing organism," said Patrick Duffy, chief of the malaria immunology laboratory at the National Institute for Allergy and Infectious Diseases. "It can swim. It can glide on a surface. It can enter a cell and pass out the other side. And it does this

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because it's constantly changing."

Duffy himself contracted malaria repeatedly while doing field work in Kenya and Tanzania. It left him with fever and stomach cramps, and made him sleepless for up to three days at a time.

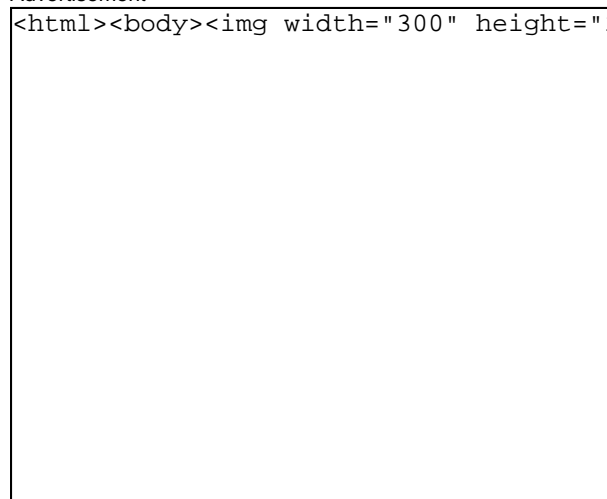
"I only had it four times," Duffy said. "But imagine living in community where everyone is infected every season." Duffy was reinfected by separate mosquito bites, but if an infection is not treated properly right away, the parasite can return weeks or months later.

"It's a debilitating and deadly disease," he said, "but it doesn't have the constituency in the developed world that other diseases have."

Walter Reed begins the next round of malaria clinical trials this fall, Ockenhouse said: "We're always looking for volunteers." (To learn about volunteering, go to <http://armyclinicaltrials.com>.)

Niiler is a freelance journalist based in Washington.

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